

# Ecoepidemiological Aspects of American Cutaneous Leishmaniasis in the State of São Paulo, Brazil

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*The aim of this study is to review some of the ecoepidemiological aspects of american cutaneous leishmaniasis (ACL) in the State of São Paulo, Brazil. During the first half of this century ACL occurred in São Paulo, predominantly on the bank of the Tietê River, where there were railroad constructions and there was inevitable contact between workers and forested areas. Man's activities resulted in a drastic reduction of the forested regions of the State and molded the present landscape found in São Paulo, which brought a gradual change in the epidemiology of ACL during this century. Currently ACL can be considered as an endemic disease. Nowadays, ACL is found in different regions of São Paulo State, and is no longer limited to the bank of the Tietê River. The disease occurs in all age groups and sexes. Lack of knowledge about wild reservoir hosts of Leishmania (V.) braziliensis has simulated speculation about the possible role played by domestic animals (dogs and equines). Man's activities also favoured Lutzomyia intermedia a sandfly species which can clearly thrive in changed environments. L.(V.) braziliensis continues to be transmitted, even after decades of forest destruction in São Paulo.*

Key words: American cutaneous leishmaniasis - epidemiology - ecoepidemiological aspects - State of São Paulo

The leishmaniasis are parasitosis caused by different species of protozoan, all of which belonging to the *Leishmania* genus.

Most of *Leishmania* species are considered to be parasites from wild animals, and less frequently of domestic animals. With a few exceptions leishmaniasis is essentially zoonotic disease (Lainson 1983, Mello 1991).

The dermatological forms caused by this protozoan in the New World are referred as american cutaneous leishmaniasis (ACL). The ACL is of great importance as a public health problem in Brazil, either because of the extensive geographical distribution or the degree of destruction observed in cutaneous or mucocutaneous lesions.

According to Terra and Crisciuma cited by Pessôa and Barretto (1948) since 1913 the presence of the disease has been parasitologically demonstrated all over Brazilian States.

Silveira (1919) concludes that from Breda's clinical report in 1895 we can recognize that ACL has been present in the interior of São Paulo since at least 1884.

Initially two aspects were recognized as being closely related to the transmission of ACL; the first one referred to the necessity of contact bet-

ween man and forested or recently deforested areas; thus Brumpt and Pedroso (1913), proposed the name "American Leishmaniasis of Forests"; the second was the possible participation of insects in the transmission of *Leishmania* to man (Lindenberg 1909).

ACL can be considered originally as a zoonotic disease, of forest environments, without man's participation and as such coincides with the concept of natural nidality of diseases as proposed by Pavlosky (1965). Gomes et al. (1990) suggest this ecological condition could explain why the relationship man-forest is a decisive factor for the occurrence of ACL.

Among the aspects related to environmental landscapes, special attention must be given to the vegetation. Although the landscape can be affected by several external factors; Humboldt (1808) pointed out that the determining scenic feature is the vegetation, which can soften uneven land or emphasize an hidrographic networks by the presence of riverine forests. Besides of this it provides the macro, microclimatic and pedologic conditions that determine the environment where biological interrelationships occur.

In a study conducted by Troppmair (1969), the primitive vegetation of the State of São Paulo, which has 248,820 km<sup>2</sup> area, was composed of 190,000 km<sup>2</sup> (76.4%) of forest, mainly on the occidental, crystalline plateau of the Paraíba River Valley, Mantiqueira Mountain, and central area of paleozoic depression; 8,400km<sup>2</sup> of meadow;

26,500 km<sup>2</sup> of clean fields; 1,600 km<sup>2</sup> of araucaria; 7,000 km<sup>2</sup> of transition zone meadow-clean fields, and 14,000 km<sup>2</sup> of seashore vegetation.

In 1907-1908, the clinical reports of ACL intensified in people from the western part of the State, where the vegetation was estimated to cover about 58.0% of São Paulo. Man's contact with the forest resulted in deforestation and the modification of the natural environment. The principal activities were the opening of new railroads, projects involving the extraction of natural products and the expansion of the coffee growing areas.

In the beginning of this century, the number of cases of ACL increased quickly in São Paulo, running along of the railroad constructions which at that time demanded the relationship between workers and forested areas. In the northwest region, ACL spread from Bauru and Araçatuba, extending to the Sorocabana region from the city of Presidente Prudente, and late, during the 1930's, in the Paulista area from Marília and Tupã always on the Tietê River's left bank as for as the Paraná River (Pessôa 1956).

Man's activities inevitably resulted in a drastic reduction of the natural vegetation of the whole São Paulo, which was estimated to be 44.8% in 1920 and only 26.2% in 1935. The occurrence of ACL was less well studied in the State of São Paulo but Brumpt and Pedroso (1913), Takaoka (1928), Pestana et al. (1939) did carry out some restricted investigations. Silveira (1919) and Barbosa (1936) tried to evaluate the distribution and general dissemination in the State using the statistics of patients examined in the Santa Casa Hospital of São Paulo capital.

In an effort to understand the spread of ACL, Pessôa and Pestana (1940), used questionnaires that were sent to 72 Health Centers located in different regions. After considering the previous reports of Silveira (1919) and Barbosa (1936), Pessôa and Pestana (1940a) proposed a distribution map of ACL in São Paulo, and classified the regions as being either a high or low endemicity or as areas where the disease was sporadic or unknown.

Subsequent studies carried out by Pessôa and Barretto (1948), led them to propose a division of the State of São Paulo in two regions: (a) high endemic region - rural area of Alta Paulista, northwest and Alta Sorocabana, which coincided with the areas of intensive deforestation during the first half of this century; (b) regions in which were rare or absent - the rest of the State.

Later as environmental changes continued, the apparent fall in the transmission rate appeared to be related to the extraordinary reduction of the natural vegetation, which in 1952 was evaluated

to have been reduced to 18.2% of the State's total area.

As soon as new areas were colonized and established, deforestation ceased, and with the end of the great forested areas occurred and the appearance of new autochthonous cases of ACL almost came to an end.

In 1951, Sampaio pointed out that "following the rhythm of deforestation, in a few years Leishmaniasis will disappear from our State". This statement was justified at the time by the complete absence of medical or scientific reports of ACL, "almost extinct" since the 1940's.

Only in late 1950's were new case of ACL described in São Paulo and it was at this point that Forattini and Oliveira (1957) registered a focus of eight cases in southern region of the State. After that, other sporadic cases were reported by Almeida Neto and Proença (1960), Arruda Zamith (1960), Bechelli et al. (1961), Forattini et al. (1972a, 1973b).

It is interesting to observe that the natural vegetation was estimated to have decreased from 12.7 to 8.3% of the total area of the State between 1962 and 1973. During this period it should be pointed out that there were reports of cases of ACL in rural areas of the cities located in residual forests, on the other hand, there were also cases in the region of the capital of the State.

A total of 189 ACL cases were notified to the Public Health Secretary of the State of São Paulo between 1975 and 1978, and 124 of them were in 1978 (CIS 1985). This coincided with the outbreak of ACL in Ribeira Valley region, which is presently the southern limit of ACL in the State and the disease was considered from that time as one of those whose notification is compulsory.

The "tool" used to evaluate whether or not cases are autochthonous is a questionnaire and even though it has some deficiencies relatively high levels have been registered. This is surprising when we consider that twenty or thirty years ago it was thought that ACL would disappear from São Paulo in consequence of man's effect on the forest which so far has been considered as indispensable if a region is to remain endemic.

The epidemiological pattern of ACL transmission in São Paulo is clearly endemic for the period from 1979 to 1993. Presently, it is remarkable that there are sporadic cases in foci which are spread throughout greater part of the State and they are no longer restricted to areas of recent colonization as described in explosive epidemics at beginning of this century.

Although the epidemiological pattern is characterized by the occurrence of sporadic cases and microfoci, the number of new ACL cases has been increasing every year as new areas in different regions have been recognized as having autochthonous cases (Wanderley et al. 1990).

From 1979 to 1992, 3,389 cases of ACL were notified in São Paulo, of which more than 70% were autochthonous (Table I). Predominantly the lesions were cutaneous, but reports of mucosal forms in 20-25% patients worrying (Table II).

In 1977, the general coefficient of ACL incidence per 100,000 inhabitants in São Paulo was 0.05. In 1993, based on partial information from the "Alexandre Vranjac" Epidemiological Surveillance Center of the São Paulo Public Health Secretary, for the first semester it is possible to project a coefficient of incidence in the order of 1.30 or 1.40 per 100,000 inhabitants.

In 1919, Silveira pointed out that only 6% of total cases of ACL were in women. Between 1979 and 1992 it was impossible to find any sex preference, the respective incidence being of 57.2 and 42.8%, for men and women.

As far as the distribution of notified ACL cases is concerned, it can be seen from Table III that in the period from 1979 to 1992 infection occurred in all age groups, and emphasizing that approximately 20% of patients were under fifteen years old. This observation contrasts to Silveira's

report in 1919, where it was observed that only 1% of the patients were under 10 years old.

The present vegetation of the State differs completely from that of the primitive landscape. Areas recognized as reserves of residual forest of varying sizes occupy less than 4 or 5% of total territorial area of the State.

Man's activities decisively modified the landscape of São Paulo, and at the same time they brought about a decisive pressures that gradually changed the epidemiology of ACL throughout this century.

Nowadays, the disease is no more restricted to men nor to certain age groups nor is it related to a particular activity which demands contact with forested areas (Tolezano et al. 1980, Gorla et al. 1993). This parasitic disease can be found in different regions of the State and is no longer limited to the bank of Tietê River, as initially noted by Pessôa and Pestana (1940a). It is associated with almost all the areas of residual forest and almost all of the rivers that pass through the State, especially the Ribeira, Mogi-Guaçu and Tietê River valleys.

According to Gomes (1992), this new epidemiological feature of ACL in São Paulo results in a lower incidence than the one reported at the beginning of this century; on the other hand, the remarkable increase of geographical distribution suggests that the risk of infection to residents in endemic areas is probably equal.

The State of São Paulo is divided into five Health Coordination Regions (HCR) (Fig.). HCR-1 includes the region composed of Greater São Paulo, with an urbanization index up to 97.0%, with sporadic isolated cases in the periferical zones along the left bank of Tiete River. HCR-2 includes several cities, all of them located on the left bank of Tietê River. This region was responsible for 91.6% of the cases during the period between 1935 and 1939 (Pessôa & Pestana 1940a), but more recently between 1979 and 1992, only 16.2% of the total autochthonous notified cases in São Paulo were from this zone (Tables IV, V).

TABLE I

Notified and autochthonous cases of American cutaneous leishmaniasis in the State of São Paulo, Brazil, 1979-1993

Years	Notified cases	Autochthonous cases	
		No.	%
1979-1992 <sup>a</sup>	3,261	2,321	71.2
1993 <sup>b</sup>	460	-	-
Total	3,721	-	-

Source: CIS/CVE - Public Health Secretary of the State of São Paulo

<sup>a</sup>: without 128 notified cases in 1984

<sup>b</sup>: until June 1993, analysis not concluded

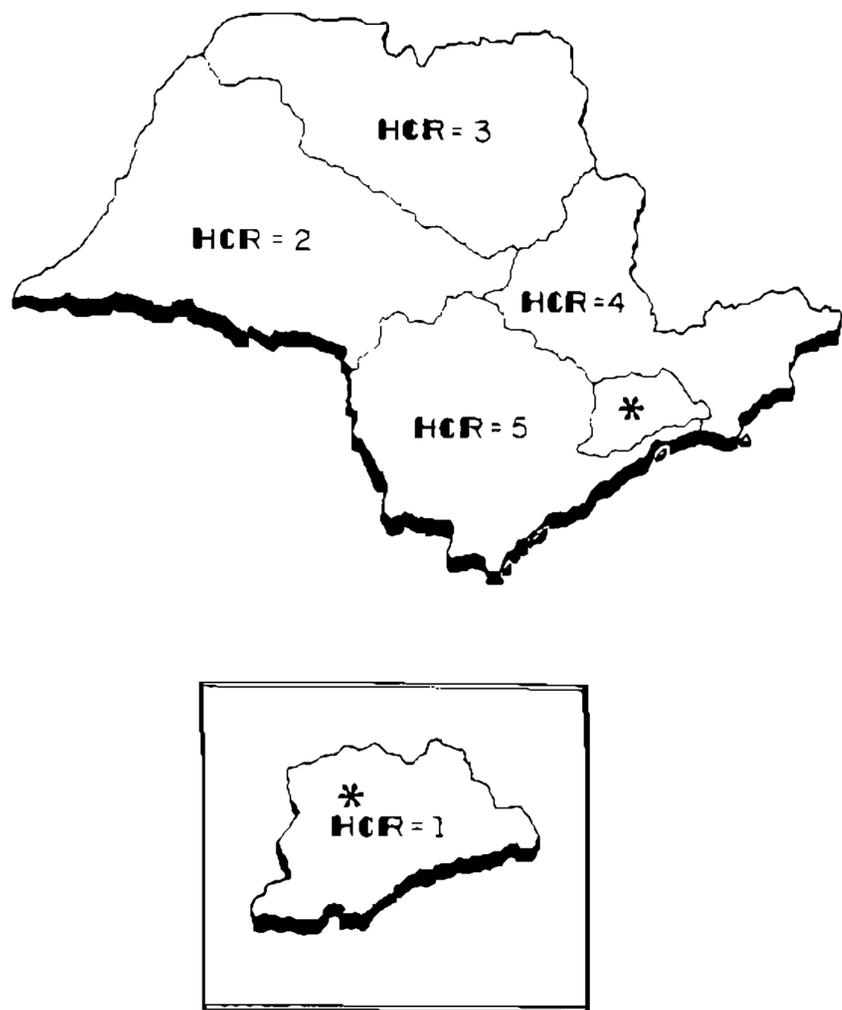
TABLE II

Distribution of American cutaneous leishmaniasis cases from the State of São Paulo, Brazil, according to the clinical form, 1979-1992

Clinical form Period	Cutaneous		Mucocutaneous		Mucosal		Unknown		Total
	No.	%	No.	%	No.	%	No.	%	
1979-1985 <sup>a</sup>	747	76.94	168	17.30	47	4.84	9	0.92	971
1986-1992	1,735	75.76	363	15.85	182	7.95	10	0.44	2,290
Total	2,482	76.11	531	16.28	229	7.02	19	0.58	3,261

Source: CIS/CVE - Public Health Secretary of the State of São Paulo

<sup>a</sup>: without 128 notified cases in 1984



Division of the State of São Paulo into Health Coordination Regions (HCR).

More recently, some of the new ACL autochthonous cases have come from HCR-3 (Tables IV, V).

HCR-4, is crossed by two important rivers; the Paraíba and Mogi-Guaçu, but the number of cases in this area were only 0.3% of those

reported between 1935-1939 (Pessoa & Pestana 1940a). Undoubtedly, HCR-4 is the region that shows the greatest increase in the coefficient of incidence, and the greatest distribution of the disease, especially along Mogi-Guaçu River, which crosses the State perpendicularly. Between 1979-1983 this region contributed with 7.92% of the cases of the State; 19.26% between 1986-1988, reaching to 25.42% between 1989-1992 (Tables IV, V).

HCR-5 includes the Sorocaba region and the Ribeira Valley. The Ribeira Valley region was considered as a non-endemic region of ACL during the first half of this century. Between 1979 and 1992 HCR-5 was, however, responsible for 60.2% of total autochthonous cases of the State (Tables IV, V).

Studies carried out in the last two decades have made it possible to recognize a new epidemiological feature of ACL in São Paulo, where transmission occurs in the domiciliary and peridomiciliary level (Tolezano et al. 1980, Rocha e Silva et al. 1980, Gomes et al. 1980, Gomes 1992).

Little is known about the specific identification of aetiological agents responsible for 300 to 400 human cases of ACL notified every year in the State. Investigations on strains isolated from a few patients have so far all been identified as *Leishmania (Viannia) braziliensis* (Tolezano et al. 1980, 1988b, 1991a,b, Yoshida et al. 1990).

As a matter of fact up until to the end of 1970's the *Leishmania* causing both human and non-human ACL was considered as to be *L.(V.) braziliensis*, without any formal investigation. In 1979, Yoshida et al. isolated a *Leishmania* from *Didelphis marsupialis aurita*, for the first time in this State. That isolate was identified as a member of subgenus *Leishmania*.

TABLE III

Distribution of American cutaneous leishmaniasis cases in the State of São Paulo, Brazil, according to age-group and time, 1979-1992<sup>a</sup>

Age Group \ Time	1979 - 1983		1986 - 1988		1989 - 1992		Total	
	No.	%	No.	%	No.	%	No.	%
0 - 4	59	7.93	35	3.44	36	4.37	130	5.03
5 - 14	138	18.55	129	12.70	119	14.44	386	14.94
15 - 49	380	51.07	565	55.61	480	58.25	1,425	55.15
50	167	22.45	287	28.25	189	22.94	643	24.88
Total	744	100	1,016	100	824	100	2,584	100

Source: CIS/CVE Public Health Secretary of the State of São Paulo

<sup>a</sup>: without notified cases during 1984 and 1985

TABLE IV

Distribution of autochthonous American cutaneous leishmaniasis cases from the State of São Paulo, Brazil, according to the Health Coordination Region (HCR) and time, 1979-1992<sup>a</sup>

Time \ HCR	1		2		3		4		5		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
1979 - 1983	1	0.16	84	13.57	10	1.61	49	7.92	475	76.74	619
1986 - 1988	3	0.41	165	22.69	50	6.88	140	19.26	369	50.76	727
1989 - 1992	4	0.56	84	11.73	48	6.70	182	25.42	398	55.59	716
Total	8	0.38	333	16.15	180	5.24	371	18.0	1,242	60.23	2,062

Source: CIS/CVE - Public Health Secretary of the State of São Paulo

<sup>a</sup>: without notified cases during 1984 and 1985

TABLE V

Distribution of autochthonous American cutaneous leishmaniasis cases from the State of São Paulo, Brazil, according to the Health Coordination of Region (HCR) in four different studies carried out during this century

Study \ HCR	1		2		3		4		5		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
1913 - 1919 <sup>a</sup> (Silveira 1919)	109	7.37	999	67.54	189	12.78	84	5.68	98	6.63	1,479
1913 - 1935 <sup>a</sup> (Barbosa 1936)	25	2.0	1,005	80.4	88	7.04	75	6.0	57	4.56	1,250
1934 - 1939 (Pessoa & Pestana 1940)	5	0.15	3,012	91.61	141	4.29	10	0.3	120	3.65	3,288
1979 - 1992 <sup>bc</sup>	8	0.38	333	16.15	108	5.24	371	18.0	1,242	60.23	2,062
Total	147	1.82	5,349	66.21	526	6.51	540	6.68	1,517	18.78	8,079

<sup>a</sup>: patients from Santa Casa Hospital in São Paulo City

<sup>b</sup>: Source: CIS/CVE - Public Health Secretary of the State of São Paulo

<sup>c</sup>: without the notified cases during 1984 and 1985

In 1983, Machado et al. reported four isolates from humans and one from a dog as *L.(L.) mexicana*. All were from the Ribeira Valley. However, Grimaldi et al. (1989) related those findings as a possible laboratory contamination.

Recently, Tolezano et al. (1988a), isolated *Leishmania* from the heart blood puncture of on *Akodon* sp. captured in Iguape City, Ribeira Valley. This parasite's was biologically that of a member of the *Leishmania* subgenus, and from zymotaxonomy and monoclonal antibodies it was identified as *L.(L.) amazonensis* (unpublished data), a parasite with increasing geographical distribution all over Brazil.

There is little information on the non-human hosts of *Leishmania* in São Paulo. In spite of few

reports since 1960's (Forattini 1960, Forattini et al. 1972b, 1973a, Yoshida et al. 1979, 1990, Machado et al. 1983, Tolezano et al. 1988a, Gomes et al. 1990), the primary wild reservoirs have not been characterized nor the non-human sources which participate in the transmission to man.

Dogs and equines have been more frequently found infected by *L.(V.) braziliensis* in endemic areas of ACL. This fact has stimulated speculation about the possible role played by this domestic animal, even though from present knowledge they would seem to be accidental hosts as is man.

In São Paulo, there are only a few studies aimed at evaluating the natural infection of *Leishmania* genus in phlebotomines (Forattini et al.

1972c, Pessôa & Coutinho 1940, 1941, Pessôa & Pestana 1940c, Taniguchi et al. 1991). The results indicated that natural infection rates were extremely low.

In other studies the objective was to report the frequency of the species; their anthropophilic behavior; colonization in the natural environment and ecological aspects (Barretto 1943, Forattini 1953, 1954, Forattini et al. 1976, Gomes et al. 1980, 1982, 1983, 1987, Taniguchi et al. 1988, 1989, 1991, Tolezano et al. 1992). Those studies emphasized the vectorial potentiality by density and anthropophilic behavior of *Lutzomyia intermedia*, *Lu. whitmani*, *Lu. migonei*, *Lu. pessoai* and *Lu. fischeri*. All these species, except *Lu. fischeri* have been found naturally infected with promastigote.

*Lu. intermedia* has been assumed to be a possible vector of *L.(V) braziliensis* in the State of São Paulo, because of its predominancy, its ability to adapt, to open and to modified environments, and its constant presence always found in peridomiliary and domiciliary (Taniguchi et al. 1991, Gomes 1992).

It is interesting to notice that extensive studies on the phlebotomine fauna performed in areas with high incidence of ACL in São Paulo during the first half of this century indicated *Lu. whitmani*, *Lu. migonei*, *Lu. fischeri* and *Lu. pessoai* as the most anthropophilic sandflies, and not *Lu. intermedia* (Pessôa & Pestana 1940b, 1940c, Pessôa & Coutinho 1940, 1941, Galvão & Coutinho 1940, Coutinho 1940).

Once again, human activity seems to have induced decisive environmental pressures that favour *Lu. intermedia*, so that *L.(V) braziliensis* continues to circulate, even after decades of forest destruction throughout whole São Paulo.

At the beginning of this century, a man-forest relationship was a vital condition for the transmission of *Leishmania* to man, facilitating the contact with wild species of phlebotomine such as *Lu. whitmani* (Forattini 1960), that is presumed to be important in maintenance of the parasite at enzootic level.

During the second half of this century, due to the drastic reduction of forested areas, conditions were established in which *L.(V) braziliensis* was able to survive in completely modified environments.

Somehow *L.(V) braziliensis* became associated with *Lu. intermedia* which was already predominant in the peridomiliary and domiciliary habitats. This predominance could confirm synanthropic occurrence in this environment (Gomes 1992).

In conclusion there are still questions that need to be answered about ACL in São Paulo: (a) identification of the different strains and species of *Leishmania* circulating in humans, phle-

botomines, wild and domestic animals; (b) identification of the wild reservoirs of the *Leishmania* species, especially *L.(V) braziliensis*, whether or not they occur; (c) identification of the phlebotomines which play roles as major or secondary vectors in endemic areas; (d) recognition of actual role of domestic animals found naturally infected in endemic areas; (e) recognition and determination of the interrelationships of biological, ecological and biogeographical factors which may possibly contribute to the spread and "perpetuation" of ACL in São Paulo.

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